

### REMARKS

Claims 19-42 and 54-57 are pending with Claims 19, 27, 33 and 37 being amended, Claim 43 being canceled and Claims 54-57 being newly added herein. The amendments to Claims 19 and 33 have been made to clarify what is being claimed. No new matter has been added with the amendments. Support for the amendments can be found in the claims as filed and in the specification, for example at [0018].

#### Rejections under 35 U.S.C. § 103

The Examiner rejected Claims 19, 23-26, 28, 29, 31-36, 38, 39, 41 and 42 under 35 U.S.C. § 103(c) as obvious over the combination of U.S. Patent No. 6,040,194 to Chick et al. and U.S. Patent No. 6,485,703 to Cote et al. The Examiner acknowledges that Chick does not teach monitoring the *intracellular* concentration of a metabolite or analyte as presently claimed. However, the Examiner argues that the claims are obvious in view of the teaching of Cote to monitor both intra- and extra-cellular analytes. The Examiner further states that there would be a reasonable expectation of success because Cote teaches that a method for monitoring intracellular concentration may involve using different sizes of particles and that Chick teaches that selectivity can be accomplished using molecular size.

Cote teaches using different two different sizes of polymer hydrogel particles, where the smaller size is taken up by cells to allow measurement of intracellular concentrations while the larger particles measure extracellular concentrations. Chick is silent as to the size of the reagents used in its sensor and how one might alter the size of the reagents. The Examiner points to column 16, line 45 of Chick as providing a teaching that selectivity can be accomplished using molecular size. Applicant notes, however, that the referenced paragraph refers to the size of the analyte and not the size of the fluorescence reagent, and is accomplished by altering the pore size of a semipermeable membrane so that only analytes of a certain maximum size can pass through to interact with the fluorescence reagent contained within the membrane of the implantable sensor. As stated in Chick, "the analyte [can] diffuse freely into and out of the sensor, but not the fluorescence reagents." (col. 16, lines 46-47)

Accordingly, Chick teaches that choice of the proper membrane can effect size-selective movement of analytes into and out of an implanted sensor. Chick does not, however, provide any teaching as to how one might alter the disclosed fluorescence reagents or substitute them

with other fluorescence reagents so as to allow the fluorescene reagent to have a size and chemistry that would allow it to diffuse across the cellular membrane of a skin cell to allow intracellular monitoring. Accordingly, one of ordinary skill in the art would not have a reasonable expectation of success in trying to combine the teachings of Cote with that of Chick to obtain the presently claimed invention.

In view of the foregoing, it is respectfully asserted that Claims 19 and 33 are patentable. Furthermore, all claims depending directly or indirectly from Claims 19 and 33 are also patentable for at least the same reasons as discussed above for their respective independent claim, and also because each claim recites a novel and unobvious combination of elements.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, the Applicants are not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. The Applicants reserve the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that the Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

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### CONCLUSION

In view of the forgoing, the present application is believed to be in condition for allowance, and such allowance is respectfully requested. If further issues remain to be resolved, the Examiner is invited to contact the Applicant's undersigned attorney of record at the number listed below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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AMEND

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